REMARKS

Applicants thank the Examiner for the courtesy of telephonic interviews on May 7, 2004 and May 11, 2004. Dr. Gary Ashley and the undersigned applicants' representative participated. The rejections of record were discussed and it was suggested that the claims be amended to claim methods of preparing an epothilone D derivative.

Upon entry of this amendment, claims 15-17 and 29-31 will be under examination. The new claims are directed to a method of preparing an epothilone D derivative (having a methyl group at C-12 and a double bond between C-12 and C-13) by providing substrates including extender units to a non-*S. cellulosum* host cell that expresses a modified functional epothilone PKS with a modified EpoE protein. Support for the claim amendments is replete in the specification and claims as originally filed. Support for "a double bond between C-12 and C-13" in claim 45 is replete in the specification.[1] No new matter is believed to be added by the new claims.

It is submitted that the new claims are in condition for allowance. With regard to U.S. Pat. No. 6,355,459 ("Schupp") cited by the Office in connection with the previously pending composition claims, Applicants submit the following observations:

The Schupp reference provides nucleotide sequence of the *Sorangium cellulosum* epothilone synthase gene cluster. However, the Schupp reference did not describe the compounds epothilone C or D and, moreover, erroneously taught that an exogenous (non-cluster) methyltransferase gene product is required to form epothilone B, the precursor of epothilone D, both of which are characterized by a methyl group at C-12. The Schupp reference contains no teaching or suggestion that the uncharacterized non-cluster methyltransferase gene was expressed in any non-*S. cellulosum* host cell. Nothing in the Schupp reference provided any expectation of success for producing an epothilone D derivative with a methyl group at C-12 and

[1] For example, at page 33, line 23, the specification explains that the C-12-C-13 alkene is a distinguishing characteristic of "epothilone D (*or an epothilone D derivative*)" [emphasis added]. As a further example, at page 16, line 22, the specification explains that epothilones C and D differ from epothilones A and B because "they lack the C-13 hydroxyl and have a double bond between C-12 and C-13."

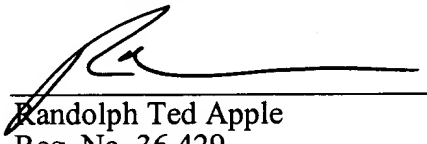
a double bond between C-12 and C-13 in a non-*S. cellulosum* host cell expressing a functional epothilone PKS with a modified EpoD protein. The present inventors described the synthesis of epothilone D and provided specific guidance about the results of particular modifications of the epoD gene (see, *e.g.*, pages 31-41 of the specification). The present inventors thus provided motivation *not found* in the Schupp reference to produce an epothilone D derivative in a non-*S. cellulosum* host cell and, further, provides an expectation of success *not found* in the Schupp references that epothilone D derivatives with a methyl group at C-12 and a double bond between C-12 and C-13 could be produced in a non-*S. cellulosum* host cell.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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